

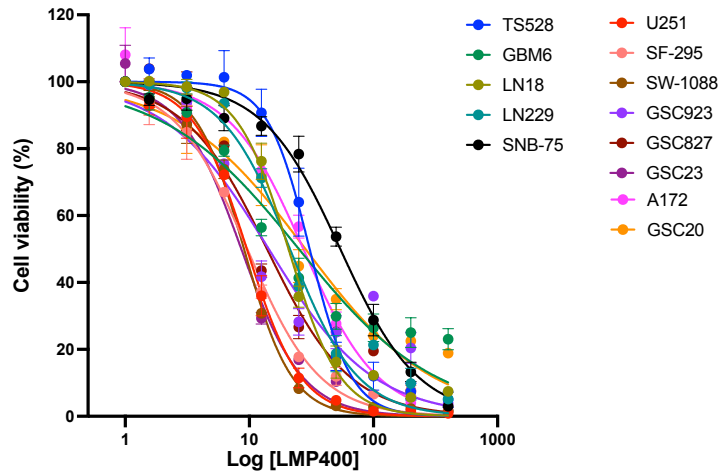
Supplementary Figures

Combined inhibition of TOP1 and PARP: a synergistic therapeutic strategy for PTEN-deficient glioblastoma

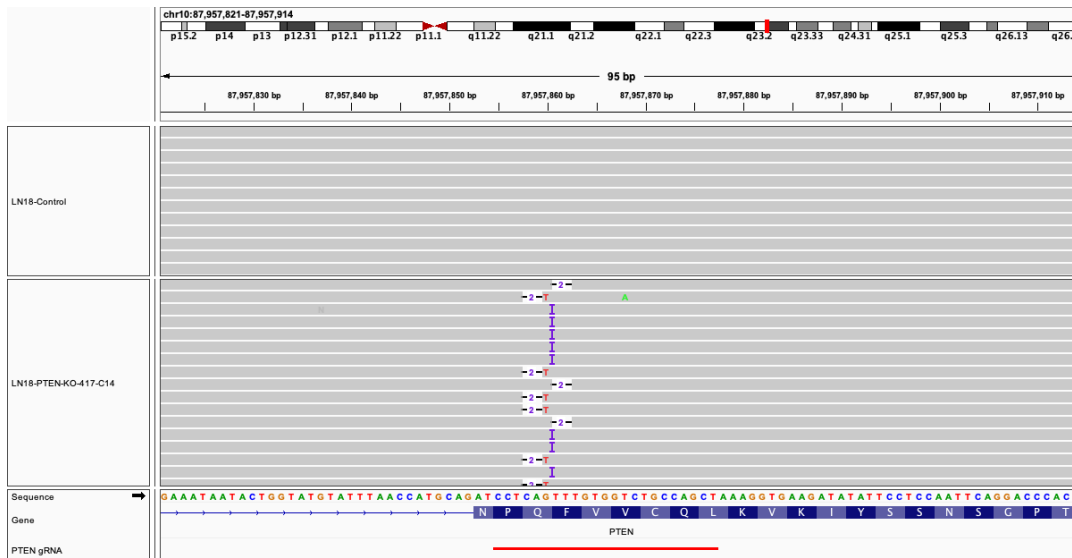
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Figure S1

A.



B.



C.

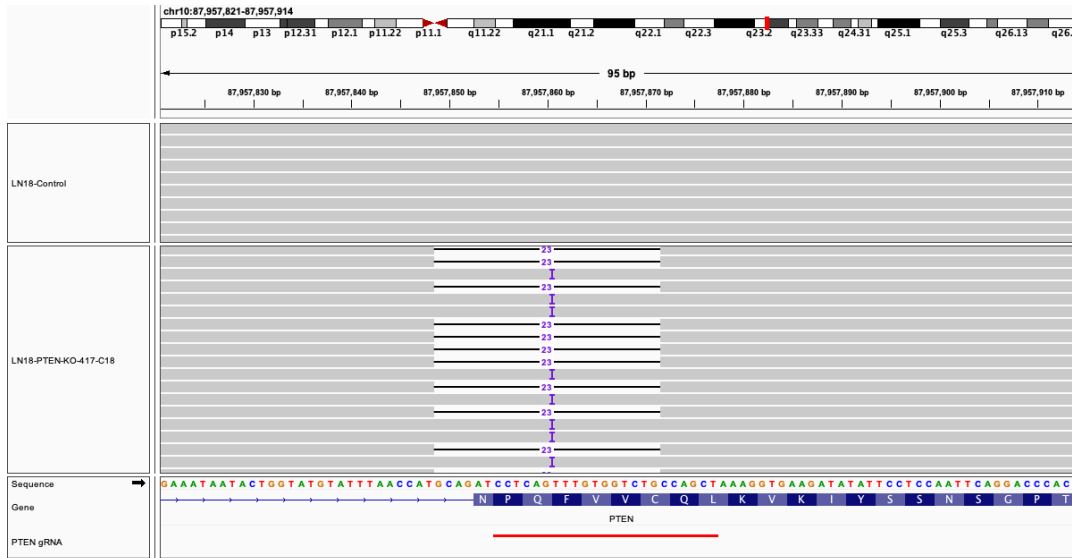


Figure S1. A. Dose response curves for LMP400 in each cell line.

Illumina deep sequencing of *PTEN* KO single clones #1 in **B** and #2 in **C** in LN18 compared to LN18-Control cells.

Figure S2

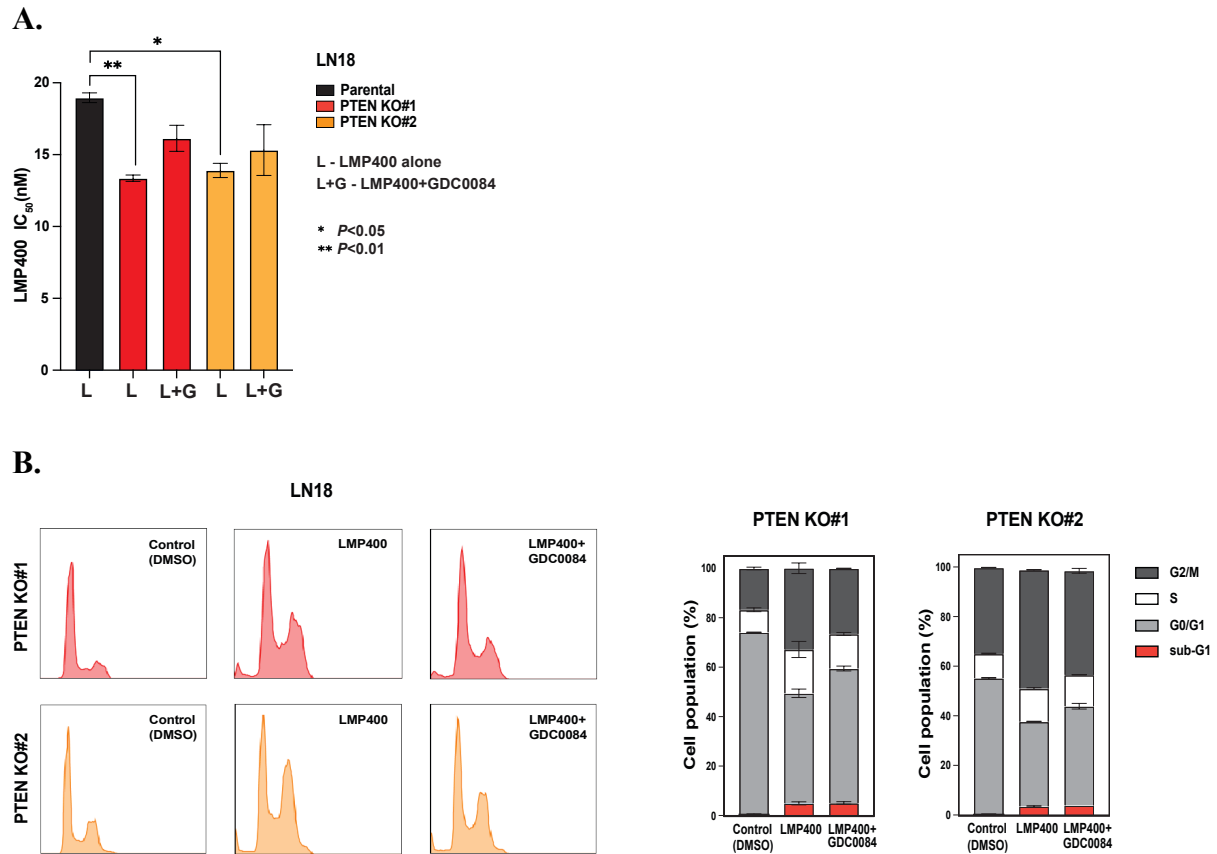


Figure S2. A. IC₅₀ of LMP400 with or without addition of GDC0084 (70 nM) in PTEN KO clones at 72 hours of treatment. **B.** Cell cycle analysis in PTEN KO clones treated with LMP400 (20 nM) + GDC0084 (70 nM) compared to those treated with LMP400 (20 nM) alone for 72 hours. A two-tailed t test was used to evaluate a difference between experimental groups.

* $p < 0.05$; ** $p < 0.01$.

Figure S3

U251		
LMP400 (nM)	Olaparib (uM)	CI Value
3	0.3	0.56293
10	1	0.41525
30	3	0.48164
100	10	0.89122
300	30	1.05498

GSC923		
LMP400 (nM)	Olaparib (uM)	CI Value
3	0.3	1.05784
10	1	0.15275
30	3	0.25407
300	30	1.02824
3000	300	0.66725

GSC827		
LMP400 (nM)	Olaparib (uM)	CI Value
3	0.3	0.98473
10	1	0.05398
30	3	0.14984
300	30	1.21691
1000	100	0.71731

SW-1088		
LMP400 (nM)	Niraparib (uM)	CI Value
3.13	0.156	0.53631
12.5	0.625	0.11531
25	1.25	0.0917
50	2.5	0.08334
200	10	0.08222

TR		
LMP400 (nM)	Niraparib (uM)	CI Value
3.13	0.156	1.03965
12.5	0.625	1.04629
25	1.25	0.52516
50	2.5	0.3597
200	10	0.43237

TRP		
LMP400 (nM)	Niraparib (uM)	CI Value
3.13	0.156	0.38863
12.5	0.625	0.27392
25	1.25	0.54173
50	2.5	0.51374
200	10	0.74167

Figure S3. CI values in each cell line calculated using Compusyn software at 72 hours post-treatment.

Figure S4.

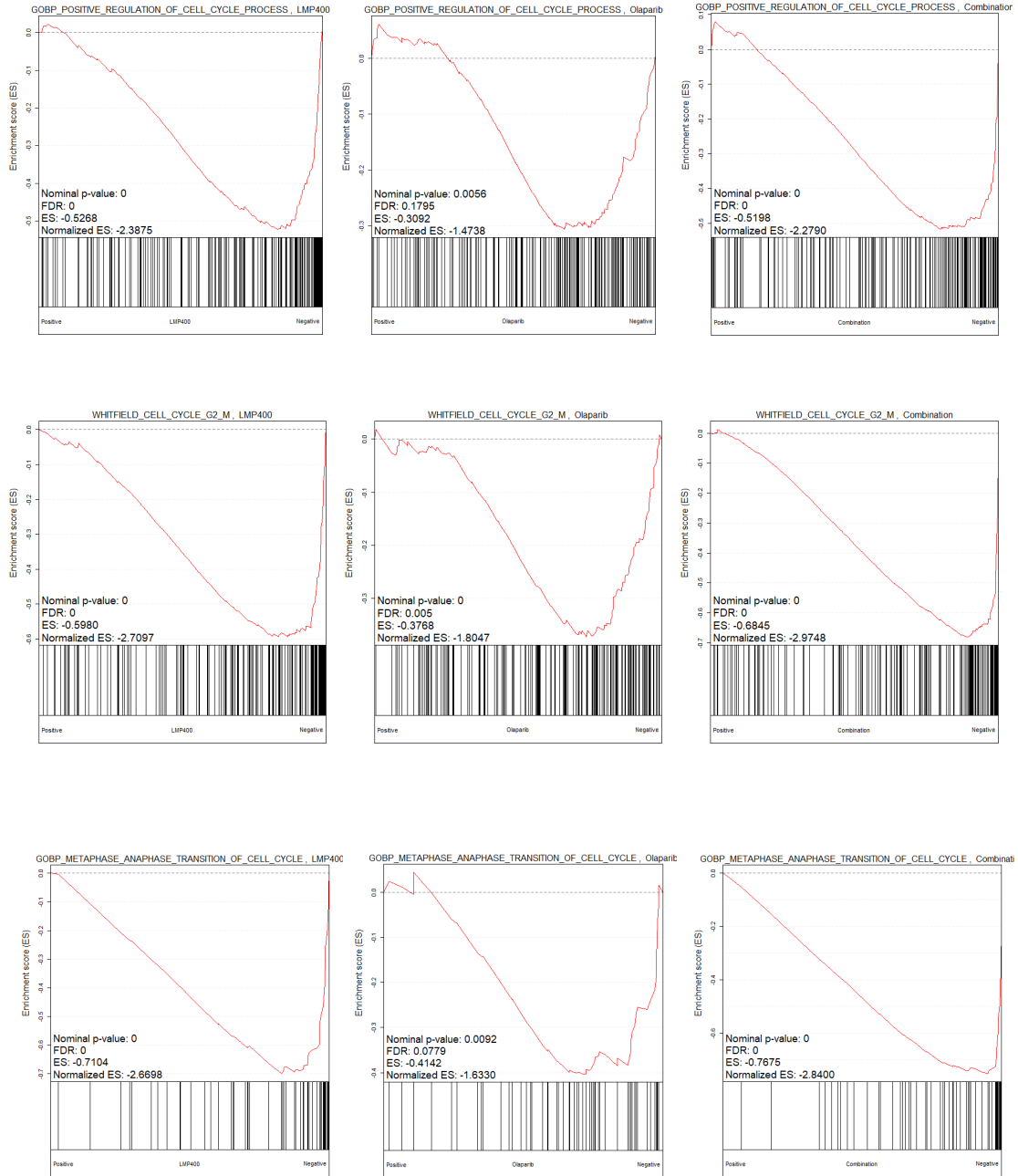


Figure S4 (continue)

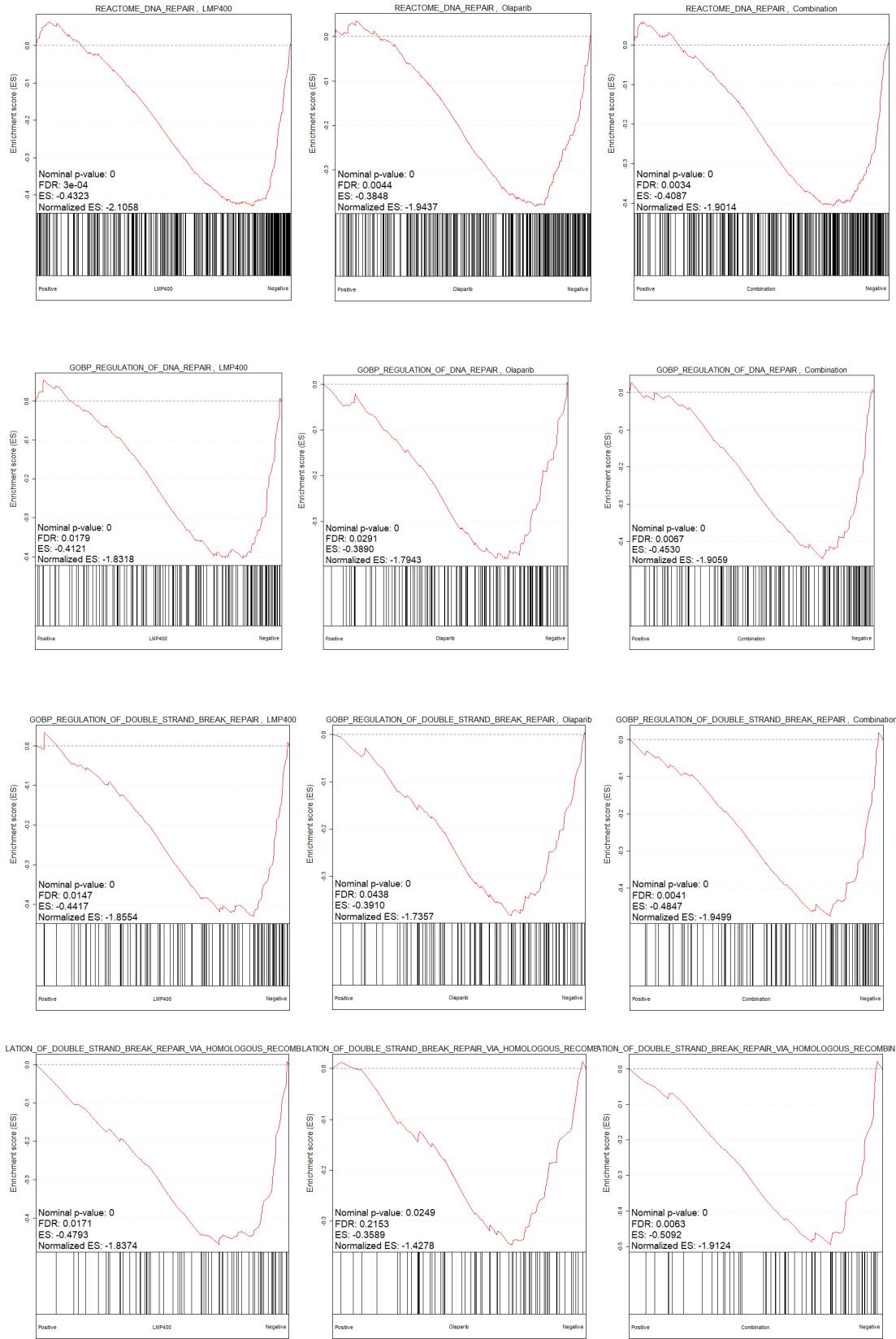


Figure S4 (continue)

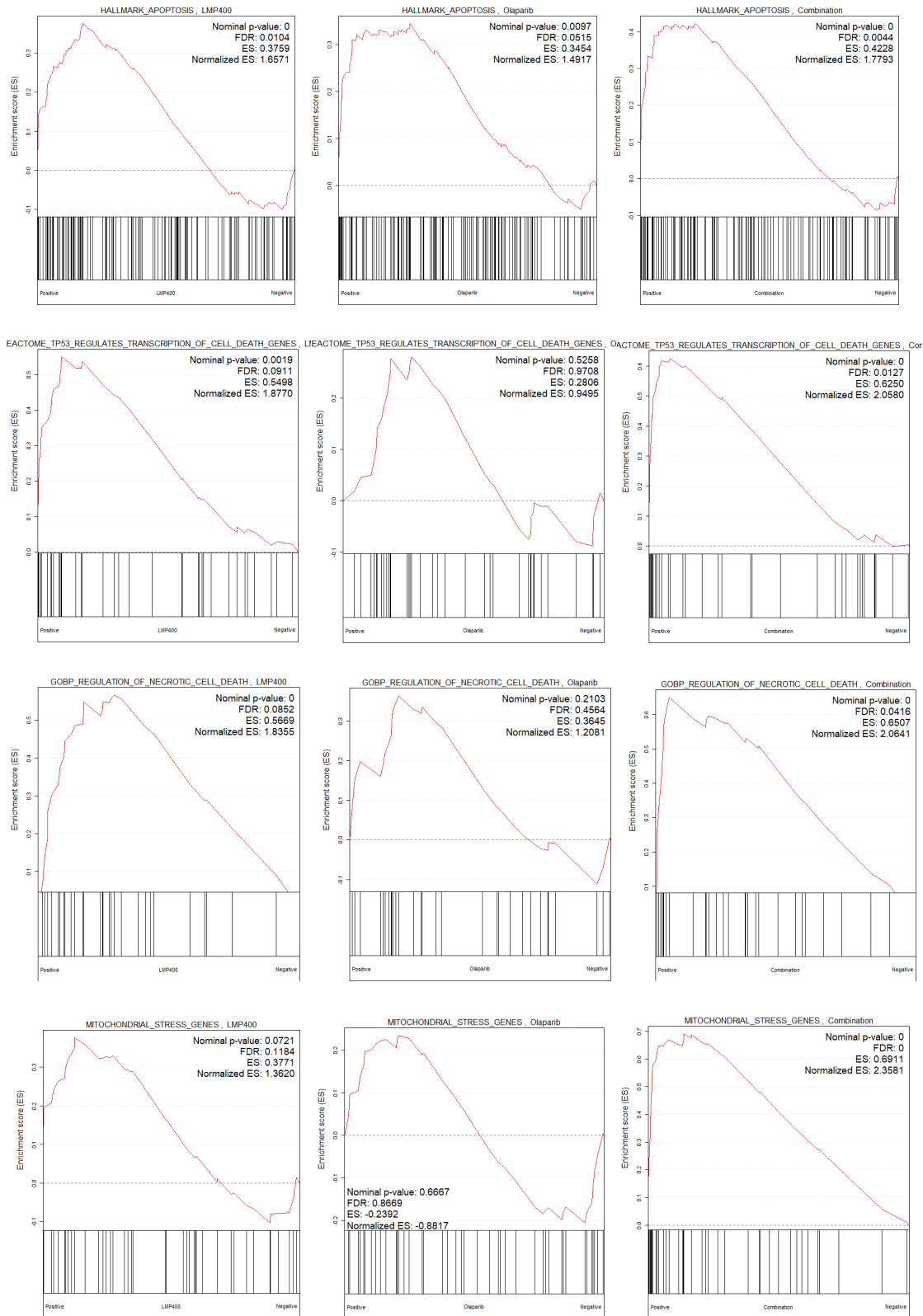


Figure S4 (continue)

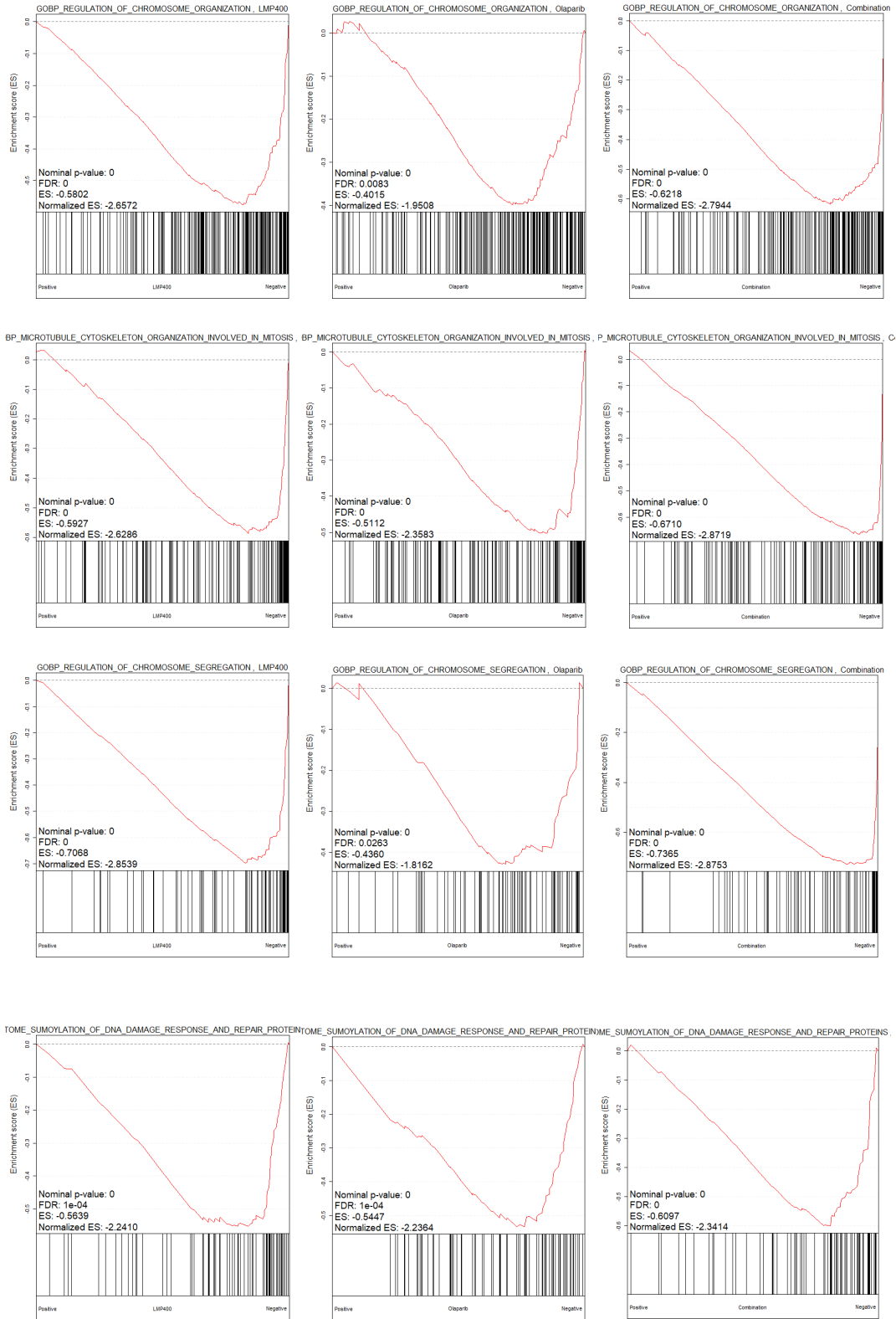


Figure S4 (continue)

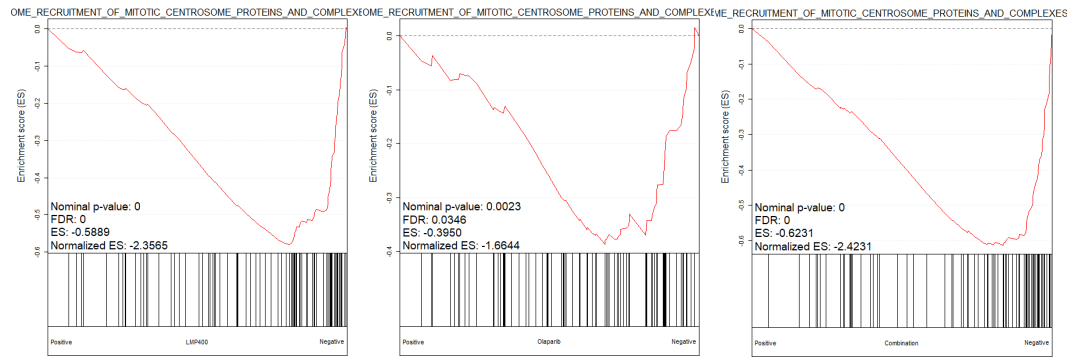


Figure S4. GSEA enrichments plots for individual dysregulated pathways per each treatment group. GSEA plots were made with the R package RToolBox.

Figure S5

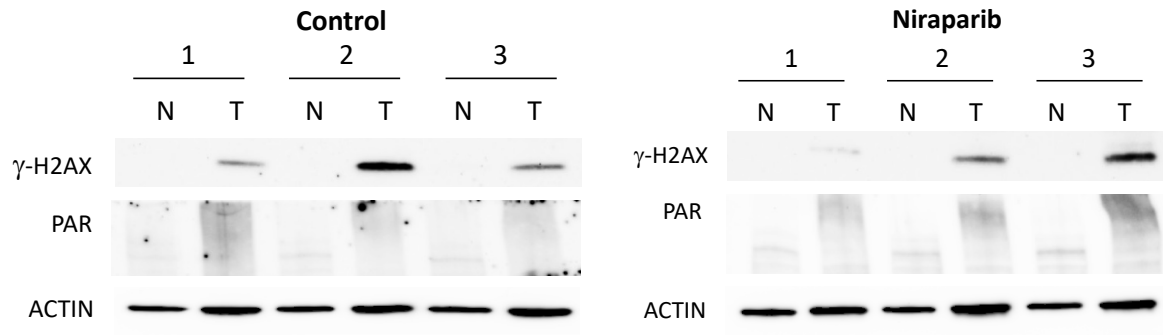


Figure S5. PD markers expression examined by Western blot analysis in mouse brain tumor and contralateral non-tumor tissues.

Figure S6

A.



B.

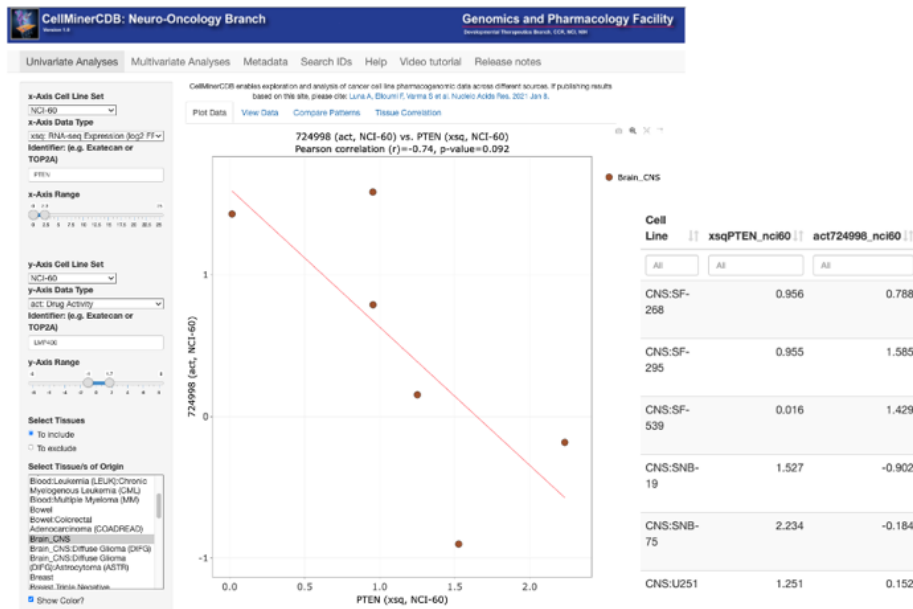


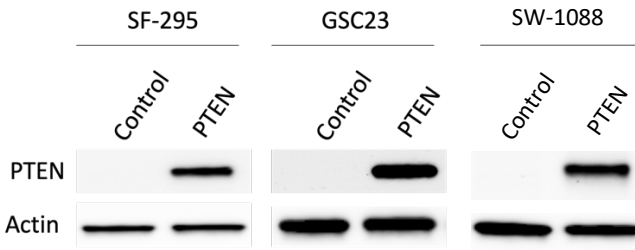
Figure S6. LMP400 (Indotecan) is more active in GBM cells with low PTEN expression.

Analysis of correlation between PTEN mRNA expression and LMP400 activity in NOB (A) and

NCI-60 (B) datasets through the CellMiner resource (<https://discover.nci.nih.gov/cellminer/>).

Figure S7

A.



B.

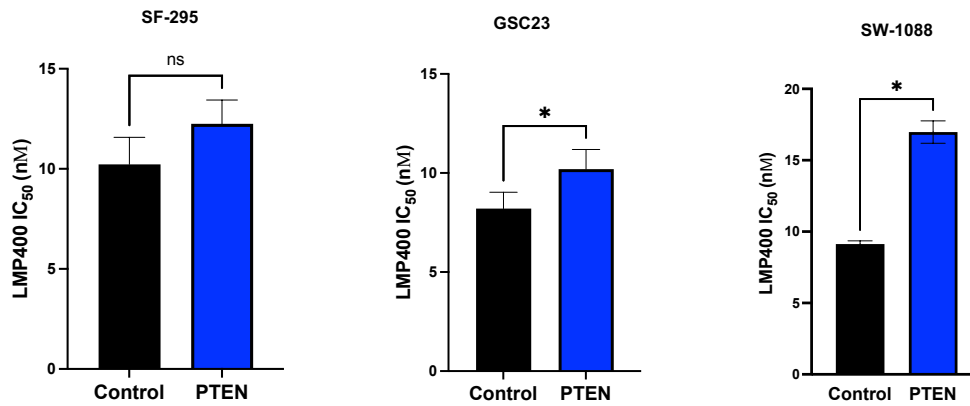


Figure S7. A. Western blot of PTEN expression rescued in SF-295, GSC23, and SW-1088 cells.

B. LMP400 IC₅₀ values in PTEN-expressing cells vs Control in SF-295, GSC23, and SW-1088

cells. A two-tailed *t* test was used to evaluate a difference between treated group and control.

**p*<0.05.